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 NEWS 14  OCT 27  DIOGENES content streamlined
 NEWS 15  OCT 27  EPFULL enhanced with additional content

 NEWS EXPRESS  JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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FILE 'BIOSIS' ENTERED AT 14:09:56 ON 09 NOV 2005

=> "FGF 1"
L1 1528 "FGF 1"

=> revascularization
L2 16827 REVASCULARIZATION

=> L1 and l2
L3 6 L1 AND L2

=> D L3 IBIB ABS 1-6

L3 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1074120 CAPLUS
DOCUMENT NUMBER: 142:32967
TITLE: Plasmid encoding fibroblast growth factor for the treatment of hypercholesterolemia or diabetes associated angiogenic defects
INVENTOR(S): Caron, Alexis; Emmanuel, Florence; Caron, Anne; Finiels, Francoise; Michelet, Sandrine; Schwartz, Bertrand; Rouy, Didier; Branellec, Didier
PATENT ASSIGNEE(S): Gencell S.a.S., Fr.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108167	A1	20041216	WO 2004-EP6903	20040604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005096286	A1	20050505	US 2004-861906	20040607

PRIORITY APPLN. INFO.:

US 2003-475959P	P	20030605
US 2004-560915P	P	20040409
US 2004-566193P	P	20040428
WO 2004-EP6903	A	20040604

AB The present invention relates to the use of a plasmid encoding a fibroblast growth factor as therapeutic agent for the prevention and treatment of hypercholesterolemia or diabetes associated myocardial or skeletal angiogenic defects. The present invention also relates to a method for enhancing formation of both collateral blood vessels and arterioles in myocardial or skeletal ischemic tissues in a mammalian subject suffering from hypercholesterolemia or diabetes. The present invention further relates to a method of promoting collateral blood vessels in ischemic myocardial or skeletal tissues without inducing VEGF-A factor expression and causing edema in the treated muscles. In particular, NV1FGF (a human **FGF-1** expression plasmid) is transferred to a rat model for hindlimb ischemia to access the potency of **FGF-1** gene transfer of therapeutic angiogenesis in ischemic skeletal muscles. NV1FGF is shown to reverse the cholesterol-induced impairment of **revascularization** in a hamster model of hindlimb ischemia by promoting the growth of both collateral vessels and arterioles in ischemic muscles exhibiting significantly decreased levels of gene expression compared with control muscles. Thus this study underscores the relevance of NV1FGF gene therapy to overcome

perfusion defects in patients with PAD.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:925484 CAPLUS
DOCUMENT NUMBER: 142:1091
TITLE: Human **FGF-1** gene transfer promotes the formation of collateral vessels and arterioles in ischemic muscles of hypercholesterolemic hamsters
AUTHOR(S): Caron, Alexis; Michelet, Sandrine; Caron, Anne; Sordello, Sylvie; Ivanov, Marie-Agnes; Delaere, Pia; Branellec, Didier; Schwartz, Bertrand; Emmanuel, Florence
CORPORATE SOURCE: Gencell S.A.S., Vitry-sur-Seine, Fr.
SOURCE: Journal of Gene Medicine (2004), 6(9), 1033-1045
CODEN: JGMEFG; ISSN: 1099-498X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acidic fibroblast growth factor (**FGF-1**) was identified as a potent mitogen for vascular cells, inducing formation of mature blood vessels in vitro and in vivo and represents one of the most promising approaches for the treatment of ischemic cardiovascular diseases by gene therapy. Nevertheless, and most probably due to the few exptl. models able to address the issue, no study has described the therapeutic effects of **FGF-1** gene transfer in subjects with peripheral arterial disease (PAD) exhibiting a clin. relevant cardiovascular pathol. In order to assess the potency of **FGF-1** gene transfer for therapeutic angiogenesis in ischemic skeletal muscles displaying decreased gene expression levels and sustained impaired formation of collateral vessels and arterioles, the authors developed a model of PAD in hamsters with a background of hypercholesterolemia. Hamsters fed a cholesterol-rich diet and subjected to hindlimb ischemia exhibit a sustained impaired angiogenic response, as evidenced by decreased angiog. score and histol. quantification of arterioles in the ischemic muscles. In this model, the authors demonstrate that NV1FGF (a human **FGF-1** expression plasmid), given i.m. 14 days after induction of hindlimb ischemia, promoted the formation of both collateral vessels and arterioles 14 days after treatment (i.e. 28 days post-ischemia). The authors' data provide evidence that NV1FGF can reverse the cholesterol-induced impairment of **revascularization** in a hamster model of hindlimb ischemia by promoting the growth of both collateral vessels and arterioles in ischemic muscles exhibiting significantly decreased levels of gene expression compared with control muscles. Therefore, this study underscores the relevance of NV1FGF gene therapy to overcome perfusion defects in patients with PAD.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:493523 CAPLUS
DOCUMENT NUMBER: 141:47325
TITLE: Method of producing biologically active human acidic fibroblast growth factor and its use in promoting angiogenesis
INVENTOR(S): Stegmann, Thomas J.; Kordyum, Vitaliy A.; Slavchenko, Iryna Yu.; Chernykh, Svitlana I.; Vozianov, Oleksandr F.
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 929,945.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004115769	A1	20040617	US 2003-649480	20030827
US 2002122792	A1	20020905	US 1999-358780	19990722
US 2002155532	A1	20021024	US 2001-929945	20010815
US 6642026	B2	20031104		
US 2003054492	A1	20030320	US 2002-280864	20021024

PRIORITY APPLN. INFO.:
US 1998-93962P P 19980724
US 1999-358780 A2 19990722
US 2000-225406P P 20000815
US 2001-929945 A2 20010815

AB The present invention relates to the treatment of coronary heart disease by **revascularization** therapy, and more particularly to the intramyocardial injection of a pharmaceutical composition comprising a recombinant fibroblast growth factor-1 protein or a fragment of a recombinant fibroblast growth factor-1 protein, optionally, with a physiol. glue for inducing local neoangiogenesis in ischemic myocardium. The invention also discloses methods of producing the recombinant fibroblast growth factor 1 protein and fragments. The methods involve phage-dependent delayed lysis of an Escherichia coli host cell for high-level prodn of soluble, recombinant protein. The effects of the human aFGF 154, 146, and 140 recombinant proteins on angiogenesis were compared to pure brain-derived aFGF using the model of new blood vessel formation in chicken embryo chorio-allantoic membrane. Induced neoangiogenesis was also found in the ischemic rat heart model. Recombinant **FGF-1** was used clin. in combination with coronary artery bypass graft in patients with coronary heart disease and FGF-1140 was used as sole therapy in 20 patients with coronary heart disease.

L3 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:674561 CAPLUS
DOCUMENT NUMBER: 137:196045
TITLE: Induction of neoangiogenesis in ischemic myocardium using a pharmaceutical composition containing **FGF-1** and a physiological glue
INVENTOR(S): Stegmann, Thomas J.
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002122792	A1	20020905	US 1999-358780	19990722
US 2004115769	A1	20040617	US 2003-649480	20030827

PRIORITY APPLN. INFO.:
US 1998-93962P P 19980724
US 1999-358780 A2 19990722
US 2000-225406P P 20000815
US 2001-929945 A2 20010815

AB The present invention relates to the treatment of coronary heart disease by **revascularization** therapy, and more particularly to the intramyocardial injection of a pharmaceutical composition comprising fibroblast growth factor-1 and a physiol. glue for inducing local neoangiogenesis in ischemic myocardium.

L3 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:641878 CAPLUS
DOCUMENT NUMBER: 131:252631
TITLE: Angiogenesis in cardiovascular disease: current status and therapeutic potential
AUTHOR(S): Sellke, Frank W.; Simons, Michael
CORPORATE SOURCE: Beth Israel Deaconess Medical Center, Division of Cardiothoracic Surgery and Cardiovascular Division, Harvard Medical School, Boston, MA, USA
SOURCE: Drugs (1999), 58(3), 391-396
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 34 refs. Therapeutic angiogenesis, in the form of growth factor protein administration or gene therapy, has emerged as a new method of treatment for patients with severe, inoperable coronary artery disease. Improved myocardial perfusion and function after the administration of angiogenic growth factors has been demonstrated in animal models of chronic myocardial ischemia. Recently, preliminary clin. trials using growth factor proteins or genes encoding these angiogenic factors have demonstrated clin. and other objective evidence of relevant angiogenesis. Thus, therapeutic angiogenesis has the potential to extend treatment options to patients who are not optimal candidates for conventional methods of myocardial **revascularization**.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:517402 BIOSIS
DOCUMENT NUMBER: PREV200000517402
TITLE: Induction of myocardial neoangiogenesis by human growth factors. A new therapeutic option in coronary heart disease.
AUTHOR(S): Stegmann, Thomas J. [Reprint author]; Hoppert, Thomas; Schneider, Andre; Gemeinhardt, Stefan; Koecher, Michael; Ibing, Rainer; Strupp, Gerhard
CORPORATE SOURCE: Klinik fuer Thorax-, Herz- und Gefaesschirurgie, Klinikum Fulda, Pacelliallee 4, D-36043, Fulda, Germany
SOURCE: Herz, (September, 2000) Vol. 25, No. 6, pp. 589-599. print. ISSN: 0340-9937.
DOCUMENT TYPE: Article
LANGUAGE: German
ENTRY DATE: Entered STN: 29 Nov 2000
Last Updated on STN: 11 Jan 2002
AB Currently available approaches for treating human coronary heart disease aim to relieve symptoms and the risk of myocardial infarction either by reducing myocardial oxygen demand, preventing further disease progression, restoring coronary blood flow pharmacologically or mechanically, or bypassing the stenotic lesions and obstructed coronary artery segments. Gene therapy, especially using angiogenic growth factors, has emerged recently as a potential new treatment for cardiovascular disease. Following extensive experimental research on angiogenic growth factors, the first clinical studies on patients with coronary heart disease and peripheral vascular lesions have been performed. The polypeptides fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) appear to be particularly effective in initiating neovascularization (neoangiogenesis) in hypoxic or ischemic tissues. The first clinical study on patients with coronary heart disease treated by local intramyocardial injection of **FGF-1** showed a 3-fold increase of capillary density mediated by the growth factor. Also, angiogenic growth factor injection intramyocardially as sole therapy for end-stage coronary disease showed an improvement of myocardial perfusion in the target areas as well as a reduction of symptoms and an increase in working capacity. Angiogenic therapy of the human myocardium introduces a new modality of treatment for coronary heart disease in terms of regulation of blood vessel growth. Beyond drug therapy, angioplasty and bypass surgery, this new approach may evolve into a fourth principle of treatment of atherosclerotic cardiovascular disease.

=> ishchemic
L4 5 ISHCHEMIC

=> heart
L5 842646 HEART

=> 4 (l) L5
L6 127697 4 (L) L5

=> infarction

L7 . 154166 INFARCTION

=> L5 and L7
L8 80758 L5 AND L7

=> L8 and L1
L9 13 L8 AND L1

=> D L9 IBIB ABS 1-13

L9 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1166271 CAPLUS
TITLE: Combination of Enoxaparin and Fibroblast Growth Factor-1 Increases Myocardial Blood Flow and Capillary Density after Myocardial **Infarction** in Rabbits
AUTHOR(S): Geist, Andrea; Marx, Jana; Mueller, Silke; Uzan, A.; von Specht, B.-U.; Haberstroh, J.
CORPORATE SOURCE: Department of Surgical Research, University Hospital Freiburg, Freiburg, Germany
SOURCE: European Surgical Research (2005), 37(4), 191-198
CODEN: EUSRBM; ISSN: 0014-312X
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: The effect of enoxaparin and fibroblast growth factor-1 (**FGF-1**) on post-**infarction** capillary d. and regional myocardial blood flow (RMBF) was examined Methods: New Zealand White rabbits received an intramyocardial injection of either physiol. saline, **FGF-1** enoxaparin, **FGF-1** or enoxaparin directly after ligation of the left anterior descending artery. RMBF and capillary d. were investigated using fluorescent microspheres and histol. examination Results: One week after **infarction** a significant difference in the number of capillaries could be demonstrated within the **FGF-1** enoxaparin group ($p < 0.001$ vs. the control group), the **FGF-1** group ($p < 0.01$) and the enoxaparin group ($p < 0.05$). Treatment with **FGF-1** enoxaparin resulted in a significantly increased number of capillaries compared to treatment with **FGF-1** ($p < 0.05$) and enoxaparin ($p < 0.05$) alone. Addnl., all groups treated with **FGF-1** and/or enoxaparin showed a significant increase of microvessel d. in the treated ischemic border zone compared to the non-treated ischemic border zone ($p < 0.001$ for **FGF-1** enoxaparin, $p < 0.01$ for **FGF-1**, $p < 0.05$ for enoxaparin). RMBF was significantly increased within the **FGF-1** enoxaparin group compared to the control group ($p < 0.05$). Moreover, perfusion rates within the **FGF-1** enoxaparin-treated area did not significantly differ from the pre-**infarction** values. Conclusion: Treatment with either enoxaparin or **FGF-1** or **FGF-1** enoxaparin resulted in increased microvessel growth. However, only the combination of enoxaparin with **FGF-1** promotes capillary growth and RMBF. Thus, we conclude that enoxaparin enhances the angiogenic potential of intramyocardially injected **FGF-1** in the acutely infarcted rabbit **heart**.

L9 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1050469 CAPLUS
DOCUMENT NUMBER: 143:339963
TITLE: Combination growth factor therapy and cell therapy for treatment of acute and chronic **heart** disease
INVENTOR(S): Franco, Wayne P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of U.S. Ser. No. 731,197.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005214260	A1	20050929	US 2004-991592		20041118
US 2002058612	A1	20020516	US 2001-828330		20010406
US 6759386	B2	20040706			
US 2004116349	A1	20040617	US 2003-730831		20031209
US 2004167070	A1	20040826	US 2003-731197		20031209
PRIORITY APPLN. INFO.:			US 2000-195624P	P	20000406
			US 2001-828330	A3	20010406
			US 2003-731197	A2	20031209

AB Acute and chronic **heart** disease is treated using a rational, multi-tier approach. A patient is pretreated with growth factor proteins or gene therapy, followed by the administration of adult stem cells. The progress of treatment is continuously monitored by echo-cardiogram with growth factor treatment and/or stem cell administration adjusted according to the results of the echo-cardiogram or clin. status of the patient. **Heart** disease is also treated by a method that comprises administration of a therapeutically effective amount of a growth factor protein by oral inhalation therapy.

L9 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:634960 CAPLUS
DOCUMENT NUMBER: 138:11587
TITLE: Angiogenesis-independent cardioprotection in **FGF-1** transgenic mice
AUTHOR(S): Buehler, Alexandra; Martire, Alessandra; Strohm, Claudia; Wolfram, Swen; Fernandez, Borja; Palmen, Meindert; Wehrens, Xander H. T.; Doevendans, Pieter A.; Franz, Wolfgang M.; Schaper, Wolfgang; Zimmermann, Rene
CORPORATE SOURCE: Department of Experimental Cardiology, Max-Planck-Institute, Bad Nauheim, D-61231, Germany
SOURCE: Cardiovascular Research (2002), 55(4), 768-777
CODEN: CVREAU; ISSN: 0008-6363
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: This study was performed to evaluate the cardioprotective role of acidic fibroblast growth factor-1 (**FGF-1**) in transgenic mice with cardiac-specific overexpression of human **FGF -1**. Methods: Mice were subjected to coronary artery occlusion for 15-75 min with a continuously recorded 3-lead ECG. Infarct size was measured and ERK-1/2 activity was assessed by Western blot anal. Creatine kinase and lactate dehydrogenase activity as marker for cell viability were measured in isolated ventricular myocytes subjected to simulated ischemia. Results: Infarct development was markedly delayed in transgenics with first signs of myocardial **infarction** visible at 45 min after coronary artery occlusion compared to 15 min in wildtype. Maximal infarct size (60% of risk area) did not differ, but transgenics reached maximal **infarction** after 75 min compared to 45 min in wildtype animals. ECG revealed delayed Q-wave development and delayed ST-segment elevation in transgenics. Creatine kinase and lactate dehydrogenase release was significantly attenuated from isolated transgenic myocytes at 4 and 8 h after simulated ischemia. The delay in infarct development is partially due to a constitutive higher expression of the extracellular signal-regulated kinases ERK-1/2 in the myocardium of transgenics. Addnl., injection of the ERK-1/2 inhibitor UO126 decreased the cardioprotective effect of **FGF-1**. Conclusion: Cardiac specific overexpression of **FGF-1** provides cardioprotection at the level of the cardiac myocyte, independent from angiogenesis, and at least partially mediated via activation of the mitogen activated protein kinase (MAP) ERK-1 and -2.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:50685 CAPLUS

DOCUMENT NUMBER: 134:99586
TITLE: Fibroblast growth factor anti-idiotype antibodies, their production, and their diagnostic and therapeutic use
INVENTOR(S): Plouet, Jean; Jouanneau, Jacqueline; Thiery, Jean-Paul; Savagner, Pierre; Malavaud, Bernard Andre; Sordello, Sylvie
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (CNRS), Fr.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004160	A1	20010118	WO 2000-FR1952	20000706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2796073	A1	20010112	FR 1999-8779	19990707
FR 2796073	B1	20030829		
CA 2378451	AA	20010118	CA 2000-2378451	20000706
EP 1189947	A1	20020327	EP 2000-949660	20000706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003504379	T2	20030204	JP 2001-509769	20000706

PRIORITY APPLN. INFO.:

FR 1999-8779	A	19990707
WO 2000-FR1952	W	20000706

AB The invention discloses the use of **FGF-1** anti-idiotype antibodies and/or FGF-2 anti-idiotype antibodies for preparing a medicine for treating pathologies involving endothelial cells implied in an angiogenic process, either for inhibiting angiogenesis, or for promoting angiogenesis, without affecting the quiescent endothelial cells, or for preparing a diagnostic product for pathologies involving endothelial cells implied in an angiogenic process. Production of the antibodies of the invention is also described.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:359425 CAPLUS
DOCUMENT NUMBER: 131:14116
TITLE: New approaches to coronary **heart** disease: induction of neovascularization by growth factors
AUTHOR(S): Stegmann, Thomas J.
CORPORATE SOURCE: Department of Thoracic and Cardiovascular Surgery, Fulda Medical Center, Fulda, Germany
SOURCE: BioDrugs (1999), 11(5), 301-308
CODEN: BIDRF4; ISSN: 1173-8804
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 51 refs. Currently available approaches for treating human coronary **heart** disease aim to relieve symptoms and the risk of myocardial **infarction** by reducing myocardial oxygen demand (drugs), preventing further disease progression (drugs), restoring coronary blood flow either pharmacol. (thrombolysis) or mech. (angioplasty), or bypassing the stenotic lesions and obstructed coronary artery segments (surgery). Direct gene therapy, as well as gene-derived therapy, especially by angiogenic growth factors, is emerging as a potential new

treatment for cardiovascular disease. After extensive exptl. research on angiogenic growth factors, the first clin. studies on patients with coronary **heart** disease or peripheral vascular lesions are being performed. The polypeptides fibroblast growth factor (FGF) and vascular endothelial growth factor seem to be effective in initiating neovascularization (neo-angiogenesis) in hypoxic or ischemic tissues. The first clin. study on patients with coronary **heart** disease treated by local injection of **FGF-1** into the compromised underperfused myocardial tissue showed a 3-fold increase of capillary d. mediated by the growth factor. Angiogenic therapy of the human myocardium introduces a new modality of treatment for coronary **heart** disease in terms of regulation of blood vessel growth. Beyond drug therapy, angioplasty and bypass surgery, this therapy may evolve to be a fourth principle of treatment of atherosclerotic cardiovascular disease.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:798674 CAPLUS
DOCUMENT NUMBER: 130:119673
TITLE: **FGF-1**: a human growth factor in the induction of neoangiogenesis
AUTHOR(S): Stegmann, Thomas J.
CORPORATE SOURCE: Department of Thoracic and Cardiovascular Surgery, Fulda Medical Center, Fulda, Germany
SOURCE: Expert Opinion on Investigational Drugs (1998), 7(12), 2011-2015
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 25 refs. Currently available approaches for treating human coronary **heart** disease aim to relieve symptoms and the risk of myocardial **infarction** either by reducing myocardial oxygen demand, preventing further disease progression, restoring coronary blood flow pharmacol. or mech., or bypassing the stenotic lesions and obstructed coronary artery segments. Gene therapy, especially using angiogenic growth factors, has emerged recently as a potential new treatment for cardiovascular disease. Following extensive exptl. research on angiogenic growth factors, the first clin. studies on patients with coronary **heart** disease and peripheral vascular lesions have been performed. The polypeptides fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) appear to be particularly effective in initiating neovascularization (neo-angiogenesis) in hypoxic or ischemic tissues. The first clin. study on patients with coronary **heart** disease treated by local intramyocardial injection of **FGF-1** showed a 3-fold increase of capillary d. mediated by the growth factor. Angiogenic therapy of the human myocardium introduces a new modality of treatment for coronary **heart** disease in terms of regulation of blood vessel growth. Beyond drug therapy, angioplasty and bypass surgery, this new approach may evolve into a fourth principle of treatment of atherosclerotic cardiovascular disease.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:728556 CAPLUS
DOCUMENT NUMBER: 130:841
TITLE: Truncated vascular endothelial cell growth factor-related proteins, VRP-encoding adenoviral vectors, and pharmaceutical use of VRPs
INVENTOR(S): Bohlen, Peter
PATENT ASSIGNEE(S): Collateral Therapeutics, USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849300	A2	19981105	WO 1998-US7801	19980420
WO 9849300	A3	19990311		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2287538	AA	19981105	CA 1998-2287538	19980420
AU 9872502	A1	19981124	AU 1998-72502	19980420
EP 977854	A2	20000209	EP 1998-919794	19980420
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001524828	T2	20011204	JP 1998-547062	19980420
NZ 500530	A	20011221	NZ 1998-500530	19980420
NZ 514872	A	20050128	NZ 1998-514872	19980420
PRIORITY APPLN. INFO.:			US 1997-842984 A	19970425
			WO 1998-US7801 W	19980420

AB The present invention provides novel truncated forms of vascular endothelial growth factor-related proteins (VRPs) which are useful for the stimulation of angiogenesis in vitro and in vivo. The invention also provides nucleic acids encoding such novel truncated VRPs and methods of producing truncated VRPs. Pharmaceutical compns. comprising truncated VRPs and methods of gene therapy using the nucleic acids which code for truncated VRPs may be useful for the treatment of **heart** disease and for wound healing.

L9 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1998:339214 CAPLUS
DOCUMENT NUMBER:	129:63235
TITLE:	Intramyocardial infusion of **FGF-1** mimics ischemic preconditioning in pig myocardium
AUTHOR(S):	Htun, Patrik; Ito, Wulf D.; Hoefer, Imo E.; Schaper, Jutta; Schaper, Wolfgang
CORPORATE SOURCE:	Max-Planck-Inst. Physiol. Clin. Res., Bad Nauheim, D-61231, Germany
SOURCE:	Journal of Molecular and Cellular Cardiology (1998), 30(4), 867-877 CODEN: JMCDAY; ISSN: 0022-2828
PUBLISHER:	Academic Press Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Previous studies on the mRNA and protein level suggested a cardioprotective role of **FGF-1**. These presumed actions of **FGF-1** and FGF-2, as well as the underlying mechanisms, were investigated in this study. Human recombinant **FGF-1** (0.5 μg/mL, 20 μl/min) and FGF-2 (2 μg/mL) were applied by direct intramyocardial infusion (IM) for 60 min prior to a 60 min LSD-occlusion and 120 min reperfusion. Myocardial **infarction** compared to the region at risk was significantly decreased by **FGF-1** and FGF-2 treatment (**FGF-1**: 51.8%, FGF-2: 57.3% vs. control 83.4%). The increase in survival time was about 33 min. and equaled that of ischemic preconditioning. This effect was caused by the mitogenic part of the mol., since infusion of a truncated version of **FGF-1** (0.5-1 μg/mL), lacking mitogenicity but maintaining hemodynamic activity, did not induce cardioprotection (78.3% vs. control 83.4%). Suramin (0.5 μg/mL) prevented the observed cardioprotection (77.0% vs. control 83.4%) proving that the cardioprotective effect is receptor-mediated. Genistein (0.5 μg/mL), an inhibitor of tyrosine kinases, abolished the cardioprotection as well (77.2% vs. control: 83.4%). Immunohistochem. staining revealed an uptake and translocation of exogenous **FGF-1** to a (peri-)nuclear localization in

myocytes and into non-myocytes for FGF-2. The authors conclude that both **FGF-1** and FGF-2 are cardioprotective (**FGF-1** being more active on a molar basis), and mimic ischemic preconditioning. Their actions are receptor-mediated and receptor activation is involved. Uptake and transport to a (peri-)nuclear localization, seems to be a pathway of minor relevance, since it could not be blocked by tyrosine kinase receptor localization, seems to be a pathway of minor relevance, since it could not be blocked by tyrosine kinase receptor inhibition. Tyrosine kinase-coupled receptor occupation in general is not protective as demonstrated by the lack of effect with VEGF-infusion.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:538475 BIOSIS
DOCUMENT NUMBER: PREV200200538475
TITLE: Angiogenesis-independent cardioprotection in **FGF-1** transgenic mice.
AUTHOR(S): Buehler, Alexandra; Martire, Alessandra; Strohm, Claudia; Wolfram, Swen; Fernandez, Borja; Palmen, Meindert; Wehrens, Xander H. T.; Doevendans, Pieter A.; Franz, Wolfgang M.; Schaper, Wolfgang; Zimmermann, Rene [Reprint author]
CORPORATE SOURCE: Department of Vascular Genomics, Kerckhoff Clinic, Benekestr. 2-8, D-61231, Bad Nauheim, Germany r.zimmer@vascular-genomics.de
SOURCE: Cardiovascular Research, (September, 2002) Vol. 55, No. 4, pp. 768-777. print.
CODEN: CVREAU. ISSN: 0008-6363.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Oct 2002
Last Updated on STN: 16 Oct 2002

AB Objective: This study was performed to evaluate the cardioprotective role of acidic fibroblast growth factor-1 (**FGF-1**) in transgenic mice with cardiac-specific overexpression of human **FGF-1**. Methods: Mice were subjected to coronary artery occlusion for 15-75 min with a continuously recorded 3-lead electrocardiogram (ECG). Infarct size was measured and ERK-1 and -2 activity was assessed by Western blot analysis. Creatine kinase and lactate dehydrogenase activity as marker for cell viability were measured in isolated ventricular myocytes subjected to simulated ischemia. Results: Infarct development was markedly delayed in transgenics with first signs of myocardial **infarction** visible at 45 min after coronary artery occlusion compared to 15 min in wildtype. Maximal infarct size (60% of risk area) did not differ, but transgenics reached maximal **infarction** after 75 min compared to 45 min in wildtype animals. ECG revealed delayed Q-wave development and delayed ST-segment elevation in transgenics. Creatine kinase and lactate dehydrogenase release was significantly attenuated from isolated transgenic myocytes at 4 and 8 h after simulated ischemia. The delay in infarct development is partially due to a constitutive higher expression of the extracellular signal-regulated kinases ERK-1 and -2 in the myocardium of transgenics. Additionally, injection of the ERK-1/2 inhibitor UO126 decreased the cardioprotective effect of **FGF-1**. Conclusion: Cardiac specific overexpression of **FGF-1** provides cardioprotection at the level of the cardiac myocyte, independent from angiogenesis, and at least partially mediated via activation of the mitogen activated protein kinase (MAP) ERK-1 and -2.

L9 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:517402 BIOSIS
DOCUMENT NUMBER: PREV200000517402
TITLE: Induction of myocardial neoangiogenesis by human growth factors. A new therapeutic option in coronary **heart** disease.
AUTHOR(S): Stegmann, Thomas J. [Reprint author]; Hoppert, Thomas; Schneider, Andre; Gemeinhardt, Stefan; Koecher, Michael;

Ibing, Rainer; Strupp, Gerhard
CORPORATE SOURCE: Klinik fuer Thorax-, Herz- und Gefaesschirurgie, Klinikum Fulda, Pacelliallee 4, D-36043, Fulda, Germany
SOURCE: Herz, (September, 2000) Vol. 25, No. 6, pp. 589-599. print. ISSN: 0340-9937.
DOCUMENT TYPE: Article
LANGUAGE: German
ENTRY DATE: Entered STN: 29 Nov 2000
Last Updated on STN: 11 Jan 2002

AB Currently available approaches for treating human coronary **heart** disease aim to relieve symptoms and the risk of myocardial **infarction** either by reducing myocardial oxygen demand, preventing further disease progression, restoring coronary blood flow pharmacologically or mechanically, or bypassing the stenotic lesions and obstructed coronary artery segments. Gene therapy, especially using angiogenic growth factors, has emerged recently as a potential new treatment for cardiovascular disease. Following extensive experimental research on angiogenic growth factors, the first clinical studies on patients with coronary **heart** disease and peripheral vascular lesions have been performed. The polypeptides fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) appear to be particularly effective in initiating neovascularization (neoangiogenesis) in hypoxic or ischemic tissues. The first clinical study on patients with coronary **heart** disease treated by local intramyocardial injection of **FGF-1** showed a 3-fold increase of capillary density mediated by the growth factor. Also, angiogenic growth factor injection intramyocardially as sole therapy for end-stage coronary disease showed an improvement of myocardial perfusion in the target areas as well as a reduction of symptoms and an increase in working capacity. Angiogenic therapy of the human myocardium introduces a new modality of treatment for coronary **heart** disease in terms of regulation of blood vessel growth. Beyond drug therapy, angioplasty and bypass surgery, this new approach may evolve into a fourth principle of treatment of atherosclerotic cardiovascular disease.

L9 ANSWER 11 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:24530 BIOSIS
DOCUMENT NUMBER: PREV200000024530
TITLE: Impaired cardiac remodeling and function after myocardial **infarction** in **FGF-1** transgenic mice.
AUTHOR(S): Palmen, Meindert [Reprint author]; Daemen, Mat J. A. P. [Reprint author]; Buehler, Alexandra; Bronsaer, Ronald J.; Zimmermann, Rene; Smits, Jos F. M.; Doevendans, Pieter A. F. M.
CORPORATE SOURCE: CARIM, Maastricht, Netherlands
SOURCE: Circulation, (Nov. 2, 1999) Vol. 100, No. 18 SUPPL., pp. I.250. print.
Meeting Info.: 72nd Scientific Sessions of the American Heart Association. Atlanta, Georgia, USA. November 7-10, 1999.
CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 1999
Last Updated on STN: 31 Dec 2001

L9 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:523645 BIOSIS
DOCUMENT NUMBER: PREV199900523645
TITLE: Cardiac-specific overexpression of **FGF-1** doubles time-to-**infarction** following coronary occlusion-reperfusion in transgenic mice.
AUTHOR(S): Buehler, Alexandra [Reprint author]; Ito, Wulf D. [Reprint author]; Fernandez, Borja [Reprint author]; Scholz, Dimitri; Kilian, Sven A. R.; Zimmermann, Rene; Franz,

Wolfgang F.; Niemann, Heiner; Doevendans, Pieter; Schaper, Wolfgang
CORPORATE SOURCE: Max-Planck-Inst., Bad Nauheim, Germany
SOURCE: Circulation, (Oct. 27, 1998) Vol. 98, No. 17 SUPPL., pp. I144. print.
Meeting Info.: 71st Scientific Sessions of the American Heart Association. Dallas, Texas, USA. November 8-11, 1998. The American Heart Association.
CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1999
Last Updated on STN: 3 Dec 1999

L9 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:394387 BIOSIS
DOCUMENT NUMBER: PREV199900394387
TITLE: Overexpression of the human **FGF-1** delays infarct development.
AUTHOR(S): Buehler, Alexandra [Reprint author]; Fernandez, Borja [Reprint author]; Bronsaer, Ronald J. P.; Doevendans, Pieter A.; Schaper, Wolfgang [Reprint author]; Zimmermann, Rene
CORPORATE SOURCE: Max-Planck-Institute, Bad Nauheim, Germany
SOURCE: Journal of Molecular and Cellular Cardiology, (June, 1999) Vol. 31, No. 6, pp. A49. print.
Meeting Info.: Abstracts of the XXth Meeting of the International Society for Heart Research, European Section. Maastricht, The Netherlands. June 20-30, 1999.
CODEN: JMCDAY. ISSN: 0022-2828.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Sep 1999
Last Updated on STN: 28 Sep 1999